

REMARKS

At the outset, applicants thank Examiner Ton for her time and consideration of the above-identified application during the interview with the undersigned.

Claims 1, 8-9, 11 and 33-36 are pending. Claim 33 has been amended to incorporate the recitations of claim 37. As claim 37 has already been examined, applicants respectfully submit that the changes to the claims raise no new issues that would require further search and consideration of the application. At the very least, applicants respectfully submit that the amendment places the application in better condition for appeal. In this regard, applicants respectfully request entry of the present amendment.

Claims 21-32 and 37 have been canceled.

In the outstanding Official Action, claims 21-26 and 28-37 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the enablement requirement.

However, as noted above, claim 33 has been amended to incorporate the subject matter of claim 37. In that claim 37 was directed to human (as recited in independent claim 33) hematopoietic stem cells, applicants believe that claim 33 and its dependent claims satisfy the enablement requirement as acknowledged by the Office Action at the bottom of page 2.

As noted above, claims 21-32 have been canceled.

As claims 21-26 and 28-32 have been canceled, applicants respectfully request that the "new matter" rejection be withdrawn.

Claims 1, 8, 9, 11, 21-26 were rejected under 35 U.S.C. 103(a) as allegedly being obvious over HATZFELD et al in view of FORTUNEL et al. This rejection is traversed.

Applicants respectfully submit that the HATZFELD et al. and FORTUNEL et al. publications are at best cumulative to what is already disclosed in the present specification. Indeed, both publications discuss using a High Proliferative Potential-Quiescent (HPP-Q) assay. The HPP-Q assay was developed to evaluate the differentiation potential of stem cells (e.g., the multipotentiality of adult stem cells or the pluripotentiality of human embryonic stem cells). In HATZFELD, it is clear that the assay seeks to stimulate quiescent primitive progenitor cells so that cells respond to cytokines. Accordingly, those cells can then be used to study the development of the stem cells. The abstract; page 1871, col. 2, first paragraph; and Figure 7 of FORTUNEL make it clear that the HPP-Q assay is used to study the development and maturation of primitive quiescent cells by administering anti-TGF- $\beta$  to up modulate cytokines. The effect of the cytokines can then be studied. Indeed, the HPP-Q assay is a rapid differentiation culture assay used to evaluate the differentiation potential of quiescent high proliferative potential cells after activation with anti-TGF $\beta$ . In other words,

the HPP-Q assay is to be understood as a diagnostic test of the differentiation potential of cells.

The HPP-Q assay is also distinguishable from the claimed invention in that the assay utilizes a very-short term proliferation of cells that grow as colonies in a semi-solid medium, which is not suitable for carrying out the multiplication of stem cells without differentiation as recited in the claimed invention.

Thus, neither Hatzfeld nor Fortunel disclose a process of stem cell production, which allows maintaining cells in an undifferentiated state while allowing their proliferation. There is also no recognition of repeatedly practicing the steps as recited in the claims so as to increase the number of cells.

As to the excerpt "*this possibility of rendering quiescent primitive progenitors responsive to optimal combinations of cytokines can be used to improve in vitro expansion of clinical samples*", this excerpt from HATZFELD et al. indicates that the purpose is for a "*transient activation*", including differentiation. In other words, the purpose of expansion is not self-renewal. HATZFELD et al. do not teach a way to keep the proliferating cells in an undifferentiated state, nor the use of anti-TGF $\beta$  in a sequential manner with TGF $\beta$  to inhibit the differentiation of the cells.

The Supreme Court recently addressed the issue of obviousness in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct.

1727, 167 L.Ed.2d 705 (2007). While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. KSR, 127 S.Ct. at 1731.

Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." Id. As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. Id.

As neither Hatzfeld et al., nor Fortunel et al. disclose a process of stem cell production as recited in the claimed invention, applicants submit that one skilled in the art would have lacked a reason to modify the publications to obtain the claimed invention.

Indeed, a critical step in analyzing obviousness pursuant to 35 U.S.C. §103(a) is casting the mind back to the time of the invention, to consider the thinking of one of ordinary skill in the art, only guided by the publications and then-accepted wisdom in the field. Adherence to this methodology is important in cases where the invention itself may prompt an Examiner to "fall victim to the insidious effect of a hindsight syndrome, wherein that which only the invention taught is used

against its teacher." *In re Kotzab*, 217 F.3d 1365, 1369-70, 55 USPQ 2d 1313, 1362 (Fed. Circ. 2000). Thus, the fact that the prior art could be so modified would not have made the modification itself obvious unless the cited publications themselves provide a reason for the modification.

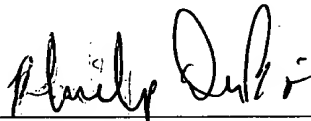
In view of the above, applicants respectfully request that the obviousness rejection be withdrawn.

Applicants believe that the present application is in condition for allowance. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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